NDA 203415/S-023
NDA 213674/S-011

SUPPLEMENT APPROVAL

Astellas Pharma US, Inc.
Attention: Ying Tu
2375 Waterview Drive
Northbrook, IL 60062

Dear Ying Tu:

Please refer to your supplemental new drug applications (sNDAs) dated August 1, 2024, received August 1, 2024, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Xtandi (enzalutamide) 40 mg capsules and 40 mg and 80 mg tablets.

These Prior Approval sNDAs propose to revise the following sections of the US Prescribing Information to add a Warning about dysphagia and choking related to product size as well as clarifying language about administration of enzalutamide capsules and tablets with a sufficient amount of water: Highlights, Dosage and Administration (Section 2.1), Warnings and Precautions (Section 5.7), Adverse Reactions (Section 6.2), Patient Counseling Information (Section 17), and Patient Information.

APPROVAL & LABELING

We have completed our review of these applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (Prescribing Information and Patient Package Insert), with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

Information on submitting SPL files using eList may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.[2]

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the carton and container labeling submitted on August 1, 2024, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved NDA 213674/S-011 NDA 203415/S-023**." Approval of this submission by FDA is not required before the labeling is used.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your supplemental applications, you are exempt from this requirement.

PATENT LISTING REQUIREMENTS

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the

[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

REQUESTED ENHANCED PHARMACOVIGILANCE (EPV)

We request that for Xtandi (enzalutamide) capsules and tablets you provide a narrative summary including analysis of the cases that describe choking or severe dysphagia due to product size, in a report submitted to your NDA as a "Clinical/Clinical Information" submission on an annual basis for 3 years following the date of this approval.

Your analysis should include interval and cumulative data relative to the date of this approval. Your analysis should provide an assessment of causality, with documentation of indication, temporal association, duration of therapy, associated signs and symptoms, confounders, underlying risk factors, treatment given for the event, outcome, and dechallenge/rechallenge. You should also provide a line listing of the cases for the reporting interval, and the search terms used to identify the cases.

Your narrative summary should include an assessment of the following, by the product form and dose/size:

- The number of cases reporting that a patient experienced choking or severe dysphagia due to product size.
- Action taken in response to choking or severe dysphagia involving Xtandi (enzalutamide), including but not limited to hospitalization status, treatments and maneuvers administered, and supportive care.
- Outcome of choking or severe dysphagia involving Xtandi (enzalutamide).
- Outcome of retreatment after choking or severe dysphagia involving Xtandi (enzalutamide) if applicable (including prior medications given and dose received).

If you have any questions, contact Alice Lee, Senior Regulatory Project Manager, at (301) 796-8881 or at Alice.Lee@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Daniel Suzman, MD
Deputy Director
Division of Oncology 1
Office of Oncologic Diseases
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert
- Carton and container labeling

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

DANIEL L SUZMAN
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